UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

MEMORANDUM

DATE: October 12, 2012

SUBJECT: **Propoxur:** Data Evaluation Record for the Study "Determination of Transferable Residues of Propoxur from the Hair of Dogs Wearing collars Impregnated with Propoxur – Final Report"

PC Code: 047802
MRID No.: 48589901
Petition No.: NA
Assessment Type: NA
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Reregistration Case No.: NA
CAS No.: 114-26-1

FROM: Shalu Shelat, Industrial Hygienist
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The purpose of this document is to provide a secondary data evaluation record (DER) for the study report "Determination of Transferable Residues of Propoxur from the Hair of Dogs Wearing Collars Impregnated with Propoxur"submitted by Wellmark International. This study measures the the amount of propoxur that may be available for transfer from a dog while the dog is wearing a Zodiac Flea Collar for Dogs, a propoxur impregnated collar (10% active ingredient). A primary review of the study was conducted by Versar Inc.

STUDY TYPE: Transferable Residues after Petting Simulations to Animal Hair

TEST MATERIAL: The test material was a propoxur impregnated flea collar, referred to as Zodiac® Flea Collar for Dogs. The flea collar contained 10% (wt/wt) propoxur.

SYNONYMS: Propoxur; RF34D; 2-(1-methylethoxy) phenyl methyl carbamate

CITATION:

Study Author:	Alice Welch, D. Chem, Wellmark International, Inc.
Title:	Propoxur: Determination of Transferable Residues from the Hair of Dogs Wearing Collars Impregnated with Propoxur – Final Report
Report Date:	August 24, 2011
Performing Laboratories:	*In-life phase*: Eurofins Agroscience Services, Inc. Sanger, CA, and Young Veterinary Research Services Turlock, CA *Analytical phase*: Wellmark International, Inc. Standards and Special Chemistry Dallas, TX
Identifying Codes:	Wellmark Protocol/Report Number 4031

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EXECUTIVE SUMMARY:

This report reviews the study "Determination of Transferable Residues from the Hair of Dogs Wearing Collars Impregnated with Propoxur" submitted by Wellmark International, Inc. The purpose of the study was to measure the transferability of the test substance from the hair of a dog wearing a propoxur impregnated collar. Each collar contained 10% propoxur (wt/wt). The collars are typically applied to dogs by securing the collar around the dog's neck and cutting off any excess collar length.

A total of 17 dogs were used in the study (2 control and 15 test dogs). Propoxur residues on cotton gloves were measured on the treated dogs after 20 petting simulations. Each simulation consisted of three strokes (60 strokes total) conducted using a mannequin hand fitted with cotton gloves over top of a nitrile glove. For the pre-application sampling interval, three cotton gloves were placed over the nitrile glove and for the postapplication simulations, five cotton gloves covered the nitrile glove. After the petting simulations were complete, the gloves were removed individually from the mannequin hand, and the nitrile gloves were discarded. Propoxur residues were extracted from the cotton gloves. Samples were

collected from each dog at the following intervals: prior to treatment, at 4 hours after treatment and at 1, 2, 4, 7, 14, 21, and 28 days after treatment.

Field fortification was conducted prior to the application and on the Day 28 sampling interval. Field fortification samples were prepared in triplicate by fortifying glove matrices at LOQ (20 µg/sample) and 100xLOQ (2004 µg/sample). All recoveries were greater than 90%; therefore, field samples were not corrected for field fortification recoveries. When residues were reported as less than the LOD (6 µg/glove) or LOQ (20 µg/glove), the registrant reported results as 0.00 µg. Versar reported these results using a finite value of ½ LOD or ½ LOQ, as appropriate. Measured residues were calculated as µg/glove, µg/cm^2 of dog surface area, and percent of application rate transferred.

Average total residues from the combined glove matrices show that maximum residues occurred four hours after application of the collars and averaged 1,626 µg/gloves. These residues are represented an average of 0.359 µg/cm^2 over the surface area of the entire dog or an average of 0.072% of the applied collar application rate. Dissipation was biphasic. Propoxur residues declined rapidly immediately after application through the first 7 days after application. From Day 7 after application to Day 28 after application, residues declined at a steady, but slower rate. Residues were 76.6 µg/gloves (0.017 µg/cm^2) by Day 28 after application.

Versar performed a dissipation kinetics analysis for propoxur. Using the individual residue data for percentage of applied dose transferable calculations collected from 4 hours through day 28 after application vs. time after application, the half-life calculated by Versar was 7.0 days (R^2 = 0.653).

The Registrant did not perform a dissipation kinetics analysis.

The following issues of concern are noted:

- Laboratory fortification samples were not analyzed at all. Typically, laboratory fortification samples are performed with each sample run as a check against losses that occur during laboratory operations (extraction, cleanup, analytical measurement). A deviation to the protocol of this study stated that "it was considered unnecessary to analyze fortification samples with each sample set because there was no interference from the glove extract with the propoxur peak.

- The strokes were collected from the same area of the dogs for each petting simulation. It is not known how this affects the percent transferable residue of samples collected in subsequent simulations.

- The characteristics of the mannequin hand were not reported, such as type of plastic and surface area.

- The USEPA Draft guidance suggests use of one sampler to ensure consistency. Two samplers were used for all intervals.

- The study was conducted using only one breed of dog.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided. The study sponsor waived claims of confidentiality within the scope of FIFRA Section 10(d) (1) (A), (B), or (C). The study sponsor and director stated that

the study was conducted under EPA Good Laboratory Practice Standards (40 CFR part 160) with no exceptions.

CONCURRENT EXPOSURE STUDY: No

WAS AIR SAMPLING CONDUCTED IN CONJUNCTION WITH SURFACE SAMPLING? No

GUIDELINE OR PROTOCOL FOLLOWED: The study was designed according to the US EPA Science Advisory Council for Exposure Draft Guidance Document for Development of Protocols to Collect Pet Fur Transferable Residues Using Mannequin Hands. It was reviewed using using applicable parts of the OPPTS Test Guidelines Series 875, Occupational and Residential Exposure Test Guidelines, Group B: 875.2100 (dislodgeable foliar residue), 875.2300 (indoor surface residue) and 875.2400 (dermal exposure). The study was designed A compliance checklist is provided in Appendix A.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test Material:

Active ingredient:	Propoxur
Formulation:	Zodiac Flea Collar for Dogs containing 10% propoxur (nominal)
Purity technical:	98.17%
Purity formulation:	9.7% to 9.76% (assayed March 4, 2011 and May 16, 2011)
Lot # technical:	ARS 10-32-PRO2
Lot # formulation:	1102117057
CAS #(s):	114-26-1
Other Relevant Information:	EPA Registration No. 2724-254

2. Relevance of Test Material to Proposed Formulation(s):

The test material appears to be the same as the product described in the proposed label for Zodiac Tick Collar for Dogs (EPA Registration No. 2724-254).

B. STUDY DESIGN

The study was conducted according to protocol for study 4031. There were two amendments to the protocol and two deviations from the protocol. The LOQ was added by Amendment #1 prior to field fortification of gloves. Amendment #2 consisted of the clarification that three gloves would be used for the pre-application petting and five gloves for all petting events after application of the collars throughout all applicable sections of the protocol. The first deviation occurred when it was considered unnecessary to analyze fortification samples with each sample set because there was no interference from the glove extract with the propoxur peak. The second deviation involved the body weight of three animals which were outside the body weight range specified in the protocol. Two test animals were below the specified minimum weight of 15 lb (6.8 kg), and one was above the specified maximum weight of 30 lb (13.6 kg).

The slightly lower and higher body weights were considered to not have an adverse effect on the study.

1. Site Description:

Test location: The study was conducted at the Young Veterinary Research Services facility in Turlock, California. The animals were housed in individual outdoor cages.

Meteorological Data: Environmental conditions were monitored using on-site weather monitoring equipment. Air temperature ranged from 35.8 to 96.4°F, and the humidity ranged from 22 to 93%.

2. Animal(s) Monitored:

Species/Breed: Beagle dogs

Number of animals in study: There were 17 dogs (8 male and 9 female) used in the study. Two of the dogs were used as control and the remaining 15 dogs were treated.

Age: The dogs were 9 to 164 months old at dose administration

Body weight: The dogs weighed 6.2 to 15.6 kg (13.7 to 34.4 lbs) at dose administration

Feeding: According to the study protocol, the maintenance procedures including feeding and access to water were to be recorded in the raw data. The field phase report did not include any information regarding feeding and water access for the dogs.

Health: All of the dogs were in good health and had not been exposed to propoxur for at least 30 days prior to the application of the collars. The dogs had no signs of skin disorders, scrapes, lesions, hair thinning, or any other malady which might have affected the study.

No clinical observations were noted in the dogs that were considered related to the treatment. During the Day 21 and Day 28 petting events, dog #5 experienced seizures immediately before petting lasting 2 minutes each time. The diagnosis was idiopathic seizure, a condition often secondary to excitement/transient hyperthermia during kennel activities. The Study Author reports that the seizures were considered highly unlikely to be related to the potential propoxur exposures. The dog was sampled on Day 21, but the Study Director opted not to sample the dog on Day 28 because the petting sample would not be representative due to the additional handling of the dog during the seizure.

No drugs or vaccines were administered during the trial and no animals died during the study.

Surface characteristics: The dogs were bathed with a non-pesticidal shampoo eight days prior to the study and were not bathed again during the study. Hair/skin observations were made twice daily. Although the observations were recorded only once daily at the beginning of the study, the second observations were recorded after this discrepancy was pointed out by the Study Director. All dogs started with medium hair density and texture with length ranging from 1.0 to 2.0 cm.

No apparent skin disorders, scrapes, lesions, hair thinning, or other malady were reported.

Other products used: None

3. Physical State of Formulation as Applied:

The test substance was applied as an impregnated plastic flea collar.

4. Application Rates and Regimes:

Application rate(s): The test product (Zodiac® Tick Collar for Dogs) is a one size fits all collar. Each collar was weighed prior to securing on the dog. Once the collar was secured the excess was cut off and weighed. The difference in the weight was referred to as the applied collar weight. The applied collar weight was multiplied by the percent active ingredient in the collar (10%) to calculate the actual dose applied. The actual dose applied ranged from 1.96 to 2.69 g ai (1,964,000 to 2,690,000 µg ai).

Application Regime: Each of the dogs was treated at the labeled rate. The collars were placed on the dogs as per label instructions. The collar was first weighed and its length measured, then it was placed around the neck of the dog. The collar was secured using the attached clasp and the excess portion of the collar was removed. One or two excess inches of the collar were left on in case an adjustment for fit was needed. The excess portion of the collar was weighed and measured and retained. The collars were applied to all of the dogs by the same person for consistency.

Application Equipment: The test substance was applied as an impregnated plastic collar around the dog's neck.

Human Safety: Research personnel wore protective gloves while handling the collars. The collars were applied to all dogs by the same person for consistency. When handling animals after installing the collar, the two handlers wore clean disposable gloves and a clean disposable apron for each dog.

5. Transferable Residue Sampling Procedures:

Method and Equipment: Five cotton gloves (three for pre-application) were placed over a powder-free nitrile glove on a mannequin hand. The cotton gloves were dye-free and 100% cotton. Two male mannequin hands, one right and one left, were utilized without prejudice. The mannequin hands were manufactured by Bendies Forms in Quebec, Canada (part number hand 405M). In order to avoid fatigue, and hence declining technique, two samplers performed the petting simulations. The researchers were randomized to the dogs for each sampling event using the RAND function in Excel.

Sampling Procedure(s): The researcher stroked the body surfaces of the dog with the mannequin hand with a uniform medium pressure and motions that ran with the lay of the hair coat. One petting simulation was comprised of three strokes

beginning from the head and ending at the tail base. The three strokes included:

- One stroke on the left side (along the ribcage)
- One stroke on the back line, not avoiding the collar.
- One stroke on the right side (along the ribcage)

Petting motions were conducted using the palmar surface of the gloved mannequin hand, with splayed fingers. Each dog was petted for 20 simulations resulting in a total of 60 strokes.

Excessive amounts of hair accumulating on the gloves due to the petting process were removed with care (after completion of the entire petting simulation).

The cotton gloves were removed one at a time by grasping the glove at the wrist and pulling the glove off the mannequin hand in such a manner as to turn the glove inside out. Each cotton glove sample was placed directly into separate clear glass jars with Teflon® lined lids for storage/extraction resulting in five samples per dog (three for pre-application) per sampling interval. The nitrile glove was discarded after each sampling interval.

Sampling Time: The length of time to complete a single stroke or the entire stroking procedure was not provided.

Replicates per surface:

- Replicates per sampling time: Seventeen dogs were sampled at each interval
- Number of sampling times: There were a total of 9 sampling intervals, including one sampling event prior to application

Times of sampling: Samples were collected prior to treatment, at 4 hours after treatment, and at 1, 2, 4, 7, 14, 21, and 28 days after treatment.

6. <u>Sample Handling</u>:

After the petting exercise, each glove sample was placed directly into separate glass jars, capped with Teflon® lined lids, placed into a plastic zipper bag, wrapped in bubble wrap, and then either placed directly into freezers, or stored on dry ice until placed into freezers. Freezer storage temperatures ranged from -30.3 to -10.7°C. Sample storage temperatures were not monitored while on dry ice. Samples were shipped by Federal Express to the analytical laboratory (Analytical Chemistry and Environmental Sciences Laboratory in Dallas, TX) in ice chests with dry ice on March 23, 28, 30, April 13, and 20, 2011. Samples were received frozen. Two samples displayed cracked sample jar lids. The lids were still on the jars secured in a plastic zip bag and wrapped in bubble wrap. The lids were replaced and the samples processed according to protocol directions. At the analytical laboratory samples were stored at <-10°C. Samples were stored for a maximum of 11 days prior to extraction.

7. <u>Analytical Methodology</u>:

Extraction method(s): The samples are brought to room temperature in the sample collection jars and extracted using 100 mL of methanol. The samples were mixed on an orbital shaker for two hours. Approximately 1-2 mL were transferred into an LC vial with a clean disposable Pasteur pipette for analysis and capped.

Detection method(s): Analysis was performed using a reverse-phase high performance liquid chromatographic method with UV diode array detection. Table 1 presents a summary of the typical operating conditions.

Table 1. Summary of Chromatographic Operating Conditions

Column	Phenomenex Synergi MAX-RP, 4 µm, 250 mm x 4.6 mm, 80 Å (11.9).
Column temperature	40°C
Flow Rate	1 ml/min
Injection volume	10 µL
Retention time	4 to 5 min
Detector	UV at 270 nm, 4nm band width; Reference 450 nm, 80 nm band width
Mobile phase	65% Acetonitrile: 35% water with a 1% acetic acid in both

Method validation: Propoxur residue measurements on cotton glove matrices were analyzed according to the method validated in the study "Method Validation of a Chemical Analysis Procedure for the Determination of Residue Levels of Propoxur on Cotton Gloves Using HPLC." The method was verified for propoxur concentrations ranging from the LOQ to 1000x LOQ. Individual recoveries ranged from 89.3% to 101%. The limit of detection (LOD) for this method is 6 µg per glove and the limit of quantitation (LOQ) was set at 20 µg per glove for propoxur.

Instrument performance and calibration: A seven-point calibration curve was prepared by injecting constant volumes of calibration standard solutions. The calibration curve was created based on linear regression. The seven propoxur standards ranged from 0.06 to 100 µg/mL.

Quantification: During HPLC analysis, quantitation of residues in all samples was achieved using an external calibration curve calculated by linear regression of instrument responses for the reference substances at multiple concentrations.

8. <u>Quality Control</u>:

Lab Recovery: It was considered by the study author to be unnecessary to analyze fortification samples with each sample set because there was no interference from the glove extract with the propoxur peak. Therefore, laboratory fortification samples were not prepared for this study.

Field blanks: Two dogs were used as controls for each sampling interval. Collars were not placed on the dogs. Both dogs were sampled using the same procedure as those wearing collars. Triplicate control glove samples were prepared during each field fortification event. Residues of propoxur were <LOD (6 µg/glove) in each of the control samples.

Field recovery: Fortifications were prepared on the day prior to application (March 21, 2011) and on the Day 28 sampling interval (April 19, 2011). Triplicate fortifications were prepared at two levels; 20 µg/sample (LOQ) and 2004 µg/sample (100xLOQ). At each fortification event, cotton gloves were placed in glass jars and the fortification solution was placed directly on each glove. After fortification the jars were capped, put in plastic zipper bags and placed into frozen storage. Fortified samples were handled, stored and shopped in the same manner as the residue samples. Field fortification recoveries are summarized in Table 2. All of the individual field fortification recoveries were >90%.

Table 2. Field Fortification Recovery for Propoxur

Interval	Fortification Level (µg/glove)	n	Percent Recovery		
			Range	Average	Standard Deviation
Cotton gloves					
Pre-Application	20	3	95.0 - 100	98.3	2.89
	2004	3	102 - 103	103	0.312
Day 28	20	3	100	100	0.00
	2004	3	97.9 – 98.9	98.3	0.500

Formulation: According to the Certificate of Analysis, the test product contained between 9.7 and 9.76% propoxur.

Tank mix: Not applicable.

Storage Stability: Prior to initiation of the field phase of the study, the stability of propoxur on cotton gloves was assessed under storage conditions over intervals of 0, 7, 14, and 21 days. Each interval consisted of three glove samples fortified at 100x LOQ (2004 µg/glove) concurrently with two fresh fortifications. Freezer storage temperatures ranged from -21.0 to -13.0°C during storage. Average percent recoveries were 101% for each of the Day 0, Day 7, and Day 14 intervals and 99.4% for the Day 21 interval. Therefore, storage stability was demonstrated for storage up to 21 days at -21.0 to -13.0°C. Actual field samples were stored at -30.3 to -10.7°C for a maximum of 11 days.

II. RESULTS AND CALCULATIONS

Observations:

- No clinical observations were noted in the dogs that were considered related to the treatment.
- Excessive amounts of hair accumulating on the gloves due to the petting process were removed.
- During the Day 21 and Day 28 petting events, dog #5 experienced seizures immediately before petting. The diagnosis was idiopathic seizure, a condition often secondary to excitement/transient hyperthermia during kennel activities. The seizures were considered highly unlikely to be related to the potential propoxur exposures.

Calculations:

Measured residues (µg/gloves) detected in each glove sample (outer and inner cotton gloves) are shown in Table 3. Field fortification recoveries were acceptable (>90%), therefore, field samples were not corrected for field fortification recoveries. When residues were reported as less than the LOD or LOQ, the registrant reported results as 0.00 µg and Versar used a finite value of ½ LOD or ½ LOQ. Versar calculated residues in µg/glove, µg/cm^2 of dog surface area, and percent of applied dose transferred.

Each sample from each sampling interval consisted of five layers of cotton gloves on a mannequin hand. The three outer gloves were assayed, and the outermost glove contained most of the residue. The second glove contained little or no residue, and no detectable residues were found on the third glove, the two inner most gloves (glove #'s 4 and 5) were not analyzed. Table 3 also provides for each replicate the total gloved mannequin hand residues (outer cotton + two inner cotton gloves) in µg/gloves, percent of applied dose transferred, and µg/cm^2 of dog surface area. Table 4 provides a summary (average and standard deviation) of these results for each sampling interval. Additionally, Figure 1 graphically shows the average percentage of the applied dose that was determined to be transferable at each sampling interval for propoxur.

The surface area of the dog was determined using the following equation as referenced from US EPA (1993) Wildlife Exposure Factors Handbook:

$$\textit{Surface area of dog (cm}^2\textit{)} = (12.3*((\textit{animal body weight (lbs)}*454)^{0.65}))$$

Average residues from three gloves combined showed that maximum residues occurred four hours after application of the collars at 1,626 µg/gloves (0.072% of applied dose and 0.359 µg/cm^2). Residues declined steadily to 76.6 µg/gloves (0.003% of applied dose and 0.017 µg/cm^2) by Day 28 after application.

Versar performed a dissipation kinetics analysis for propoxur. Dissipation was biphasic. Propoxur residues declined rapidly immediately after application through the first 7 days after application. Using the individual data points for percentage of applied dose transferable vs. time for samples collected from 4 hours through day 28 after application, the half-life calculated by Versar was 7.0 days (R^2 = 0.653).

The Registrant did not perform a dissipation kinetics analysis.

III. DISCUSSION

A. LIMITATIONS OF THE STUDY:

The following issues of concern are noted:

- The strokes were collected from the same area of the dogs for each petting simulation. It is not known how this affects the percent transferable residue of samples collected in subsequent simulations.

- Laboratory fortification samples were not analyzed at all. Typically, laboratory fortification samples are performed with each sample run as a check against losses that occur during laboratory operations (extraction, cleanup, analytical measurement). A deviation to the protocol of this study stated that "it was considered unnecessary to analyze fortification samples with each sample set because there was no interference from the glove extract with the propoxur peak.

- The characteristics of the mannequin hand were not reported, such as type of plastic and surface area.

- The USEPA Draft guidance suggests use of one sampler to ensure consistency. Two samplers were used for all intervals.

Cotton gloves were used to the collect the samples.

- The study was conducted using only one breed of dog.

B. <u>CONCLUSIONS</u>:

The Registrant and Versar calculated similar transferable residues. The slight difference is most likely due to Versar's use of ½ LOD or ½ LOQ for those values assayed at less than the LOD or LOQ. The Registrant reported total residues as the sum of detectable residues on each glove.

Table 3. Propoxur Residues from Cotton Gloves Following 20 Petting Simulations to Treated Dogs										
Interval	Animal #	Animal Weight (kg)	Animal Surface Area (cm^2)	Actual Dose Applied[1] (µg ai)	Measured Residue on Gloves (µg/glove)			Total Residue[3]		% of applied dose transferred[4]
					Outer Cotton Glove #1[2]	Inner Cotton Glove #2[2]	Inner Cotton Glove #3[2]	µg/gloves	µg/cm^2 surface area of dog	
Pre-Application	1 - control	9.70	4804	0	<LOD	<LOD	<LOD	<LOD	NA	NA
	2 - control	11.2	5274	0	<LOD	<LOD	<LOD	<LOD	NA	NA
	3	8.55	4425	2374000	<LOD	<LOD	<LOD	<LOD	NA	NA
	4	9.60	4771	2466000	<LOD	<LOD	<LOD	<LOD	NA	NA
	5	10.0	4884	2235000	<LOD	<LOD	<LOD	<LOD	NA	NA
	6	15.6	6542	2690000	<LOD	<LOD	<LOD	<LOD	NA	NA
	7	8.45	4392	2114000	<LOD	<LOD	<LOD	<LOD	NA	NA
	8	10.3	4995	2395000	<LOD	<LOD	<LOD	<LOD	NA	NA
	9	6.80	3813	1966000	<LOD	<LOD	<LOD	<LOD	NA	NA
	10	9.15	4625	2223000	<LOD	<LOD	<LOD	<LOD	NA	NA
	11	6.50	3703	2014000	<LOD	<LOD	<LOD	<LOD	NA	NA
	12	8.50	4408	2437000	<LOD	<LOD	<LOD	<LOD	NA	NA
	13	12.7	5708	2549000	<LOD	<LOD	<LOD	<LOD	NA	NA
	14	9.80	4836	2241000	<LOD	<LOD	<LOD	<LOD	NA	NA
	15	7.15	3940	2234000	<LOD	<LOD	<LOD	<LOD	NA	NA
	16	7.90	4204	2220000	<LOD	<LOD	<LOD	<LOD	NA	NA
	17	6.20	3591	1964000	<LOD	<LOD	<LOD	<LOD	NA	NA
4 hours	1 - control	9.70	4804	0	<LOD	<LOD	<LOD	<LOD	NA	NA
	2 - control	11.2	5274	0	<LOD	<LOD	<LOD	<LOD	NA	NA
	3	8.55	4425	2374000	1498	<LOD	<LOD	1504	0.340	0.06
	4	9.60	4771	2466000	1873	<LOQ	<LOD	1886	0.395	0.08
	5	10.0	4884	2235000	1215	<LOQ	<LOD	1228	0.251	0.05
	6	15.6	6542	2690000	3355	<LOQ	<LOD	3368	0.515	0.13
	7	8.45	4392	2114000	1468	<LOD	<LOD	1474	0.336	0.07
	8	10.3	4995	2395000	1262	<LOD	<LOD	1268	0.254	0.05
	9	6.80	3813	1966000	2207	<LOQ	<LOD	2220	0.582	0.11
	10	9.15	4625	2223000	770	<LOQ	<LOD	783	0.169	0.04
	11	6.50	3703	2014000	1452	<LOQ	<LOD	1465	0.396	0.07
	12	8.50	4408	2437000	1868	<LOD	<LOD	1874	0.425	0.08
	13	12.7	5708	2549000	1208	<LOQ	<LOD	1221	0.214	0.05
	14	9.80	4836	2241000	1370	<LOQ	<LOD	1383	0.286	0.06
	15	7.15	3940	2234000	1063	<LOD	<LOD	1069	0.271	0.05
	16	7.90	4204	2220000	1617	<LOQ	<LOD	1630	0.388	0.07
	17	6.20	3591	1964000	2010	<LOD	<LOD	2016	0.561	0.10
Day 1	1 - control	9.70	4804	0	<LOD	<LOD	<LOD	<LOD	NA	NA
	2 - control	11.2	5274	0	<LOD	<LOD	<LOD	<LOD	NA	NA
	3	8.55	4425	2374000	719	<LOQ	<LOD	732	0.165	0.031

Table 3. Propoxur Residues from Cotton Gloves Following 20 Petting Simulations to Treated Dogs										
Interval	Animal #	Animal Weight (kg)	Animal Surface Area (cm^2)	Actual Dose Applied[1] (µg ai)	Measured Residue on Gloves (µg/glove)			Total Residue[3]		% of applied dose transferred[4]
					Outer Cotton Glove #1[2]	Inner Cotton Glove #2[2]	Inner Cotton Glove #3[2]	µg/gloves	µg/cm^2 surface area of dog	
	4	9.60	4771	2466000	1039	23	<LOD	1065	0.223	0.043
	5	10.0	4884	2235000	435	<LOD	<LOD	441	0.090	0.020
	6	15.6	6542	2690000	1946	<LOQ	<LOD	1959	0.299	0.073
	7	8.45	4392	2114000	677	<LOD	<LOD	683	0.156	0.032
	8	10.3	4995	2395000	533	<LOQ	<LOD	546	0.109	0.023
	9	6.80	3813	1966000	1403	<LOD	<LOD	1409	0.370	0.072
	10	9.15	4625	2223000	265	<LOQ	<LOD	278	0.060	0.013
	11	6.50	3703	2014000	742	<LOD	<LOD	748	0.202	0.037
	12	8.50	4408	2437000	1546	<LOD	<LOD	1552	0.352	0.064
	13	12.7	5708	2549000	618	<LOD	<LOD	624	0.109	0.024
	14	9.80	4836	2241000	720	<LOD	<LOD	726	0.150	0.032
	15	7.15	3940	2234000	395	<LOD	<LOD	401	0.102	0.018
	16	7.90	4204	2220000	404	<LOD	<LOD	410	0.098	0.018
	17	6.20	3591	1964000	1580	<LOD	<LOD	1586	0.442	0.081
Day 2	1 - control	9.70	4804	0	<LOD	<LOD	<LOD	<LOD	NA	NA
	2 - control	11.2	5274	0	<LOD	<LOD	<LOD	<LOD	NA	NA
	3	8.55	4425	2374000	403	<LOD	<LOD	409	0.092	0.017
	4	9.60	4771	2466000	338	<LOD	<LOD	344	0.072	0.014
	5	10.0	4884	2235000	267	<LOD	<LOD	273	0.056	0.012
	6	15.6	6542	2690000	1516	<LOD	<LOD	1522	0.233	0.057
	7	8.45	4392	2114000	628	<LOD	<LOD	634	0.144	0.030
	8	10.3	4995	2395000	258	<LOD	<LOD	264	0.053	0.011
	9	6.80	3813	1966000	843	<LOD	<LOD	849	0.223	0.043
	10	9.15	4625	2223000	243	<LOD	<LOD	249	0.054	0.011
	11	6.50	3703	2014000	513	<LOD	<LOD	519	0.140	0.026
	12	8.50	4408	2437000	1037	<LOD	<LOD	1043	0.237	0.043
	13	12.7	5708	2549000	398	<LOD	<LOD	404	0.071	0.016
	14	9.80	4836	2241000	527	<LOD	<LOD	533	0.110	0.024
	15	7.15	3940	2234000	694	<LOD	<LOD	700	0.178	0.031
	16	7.90	4204	2220000	278	<LOD	<LOD	284	0.068	0.013
	17	6.20	3591	1964000	1303	<LOD	<LOD	1309	0.365	0.067
Day 4	1 - control	9.70	4804	0	<LOD	<LOD	<LOD	<LOD	NA	NA
	2 - control	11.2	5274	0	<LOD	<LOD	<LOD	<LOD	NA	NA
	3	8.55	4425	2374000	333	<LOD	<LOD	339	0.077	0.014
	4	9.60	4771	2466000	136	<LOD	<LOD	142	0.030	0.006
	5	10.0	4884	2235000	259	<LOD	<LOD	265	0.054	0.012
	6	15.6	6542	2690000	1063	<LOD	<LOD	1069	0.163	0.040
	7	8.45	4392	2114000	353	<LOD	<LOD	359	0.082	0.017

Table 3. Propoxur Residues from Cotton Gloves Following 20 Petting Simulations to Treated Dogs										
Interval	Animal #	Animal Weight (kg)	Animal Surface Area (cm^2)	Actual Dose Applied[1] (µg ai)	Measured Residue on Gloves (µg/glove)			Total Residue[3]		% of applied dose transferred[4]
					Outer Cotton Glove #1[2]	Inner Cotton Glove #2[2]	Inner Cotton Glove #3[2]	µg/gloves	µg/cm^2 surface area of dog	
	8	10.3	4995	2395000	350	<LOD	<LOD	356	0.071	0.015
	9	6.80	3813	1966000	395	<LOD	<LOD	401	0.105	0.020
	10	9.15	4625	2223000	110	<LOD	<LOD	116	0.025	0.005
	11	6.50	3703	2014000	253	<LOD	<LOD	259	0.070	0.013
	12	8.50	4408	2437000	545	<LOD	<LOD	551	0.125	0.023
	13	12.7	5708	2549000	230	<LOD	<LOD	236	0.041	0.009
	14	9.80	4836	2241000	330	<LOD	<LOD	336	0.069	0.015
	15	7.15	3940	2234000	572	<LOD	<LOD	578	0.147	0.026
	16	7.90	4204	2220000	98.0	<LOD	<LOD	104	0.025	0.005
	17	6.20	3591	1964000	992	<LOD	<LOD	998	0.278	0.051
Day 7	1 - control	9.70	4804	0	<LOD	<LOD	<LOD	<LOD	NA	NA
	2 - control	11.2	5274	0	<LOD	<LOD	<LOD	<LOD	NA	NA
	3	8.55	4425	2374000	156	<LOD	<LOD	162	0.037	0.007
	4	9.60	4771	2466000	131	<LOD	<LOD	137	0.029	0.006
	5	10.0	4884	2235000	150	<LOD	<LOD	156	0.032	0.007
	6	15.6	6542	2690000	513	<LOD	<LOD	519	0.079	0.019
	7	8.45	4392	2114000	157	<LOD	<LOD	163	0.037	0.008
	8	10.3	4995	2395000	133	<LOD	<LOD	139	0.028	0.006
	9	6.80	3813	1966000	195	<LOD	<LOD	201	0.053	0.010
	10	9.15	4625	2223000	69.0	<LOD	<LOD	75.0	0.016	0.003
	11	6.50	3703	2014000	168	<LOD	<LOD	174	0.047	0.009
	12	8.50	4408	2437000	360	<LOD	<LOD	366	0.083	0.015
	13	12.7	5708	2549000	281	<LOD	<LOD	287	0.050	0.011
	14	9.80	4836	2241000	193	<LOD	<LOD	199	0.041	0.009
	15	7.15	3940	2234000	422	<LOD	<LOD	428	0.109	0.019
	16	7.90	4204	2220000	83.0	<LOD	<LOD	89.0	0.021	0.004
	17	6.20	3591	1964000	507	<LOD	<LOD	513	0.143	0.026
Day 14	1 - control	9.70	4804	0	<LOD	<LOD	<LOD	<LOD	NA	NA
	2 - control	11.2	5274	0	<LOD	<LOD	<LOD	<LOD	NA	NA
	3	8.55	4425	2374000	209	<LOD	<LOD	215	0.049	0.009
	4	9.60	4771	2466000	65.0	<LOD	<LOD	71.0	0.015	0.003
	5	10.0	4884	2235000	100	<LOD	<LOD	106	0.022	0.005
	6	15.6	6542	2690000	358	<LOD	<LOD	364	0.056	0.014
	7	8.45	4392	2114000	176	<LOD	<LOD	182	0.041	0.009
	8	10.3	4995	2395000	72.0	<LOD	<LOD	78.0	0.016	0.003
	9	6.80	3813	1966000	123	<LOD	<LOD	129	0.034	0.007
	10	9.15	4625	2223000	42.0	<LOD	<LOD	48.0	0.010	0.002
	11	6.50	3703	2014000	161	<LOD	<LOD	167	0.045	0.008

Table 3. Propoxur Residues from Cotton Gloves Following 20 Petting Simulations to Treated Dogs										
Interval	Animal #	Animal Weight (kg)	Animal Surface Area (cm^2)	Actual Dose Applied[1] (µg ai)	Measured Residue on Gloves (µg/glove)			Total Residue[3]		% of applied dose transferred[4]
					Outer Cotton Glove #1[2]	Inner Cotton Glove #2[2]	Inner Cotton Glove #3[2]	µg/gloves	µg/cm^2 surface area of dog	
	12	8.50	4408	2437000	145	<LOD	<LOD	151	0.034	0.006
	13	12.7	5708	2549000	42.0	<LOD	<LOD	48.0	0.008	0.002
	14	9.80	4836	2241000	88.0	<LOD	<LOD	94.0	0.019	0.004
	15	7.15	3940	2234000	222	<LOD	<LOD	228	0.058	0.010
	16	7.90	4204	2220000	82.0	<LOD	<LOD	88.0	0.021	0.004
	17	6.20	3591	1964000	204	<LOD	<LOD	210	0.058	0.011
Day 21	1 - control	9.70	4804	0	<LOD	<LOD	<LOD	<LOD	NA	NA
	2 - control	11.2	5274	0	<LOD	<LOD	<LOD	<LOD	NA	NA
	3	8.55	4425	2374000	96.0	<LOD	<LOD	102	0.023	0.004
	4	9.60	4771	2466000	50.0	<LOD	<LOD	56.0	0.012	0.002
	5	10.0	4884	2235000	50.0	<LOD	<LOD	56.0	0.011	0.003
	6	15.6	6542	2690000	299	<LOD	<LOD	305	0.047	0.011
	7	8.45	4392	2114000	131	<LOD	<LOD	137	0.031	0.006
	8	10.3	4995	2395000	47.0	<LOD	<LOD	53.0	0.011	0.002
	9	6.80	3813	1966000	76.0	<LOD	<LOD	82.0	0.022	0.004
	10	9.15	4625	2223000	69.0	<LOD	<LOD	75.0	0.016	0.003
	11	6.50	3703	2014000	159	<LOD	<LOD	165	0.045	0.008
	12	8.50	4408	2437000	72.0	<LOD	<LOD	78.0	0.018	0.003
	13	12.7	5708	2549000	57.0	<LOD	<LOD	63.0	0.011	0.002
	14	9.80	4836	2241000	80.0	<LOD	<LOD	86.0	0.018	0.004
	15	7.15	3940	2234000	118	<LOD	<LOD	124	0.031	0.006
	16	7.90	4204	2220000	53.0	<LOD	<LOD	59.0	0.014	0.003
	17	6.20	3591	1964000	87.0	<LOD	<LOD	93.0	0.026	0.005
Day 28	1 - control	9.70	4804	0	<LOD	<LOD	<LOD	<LOD	NA	NA
	2 - control	11.2	5274	0	<LOD	<LOD	<LOD	<LOD	NA	NA
	3	8.55	4425	2374000	88.0	<LOD	<LOD	94.0	0.021	0.004
	4	9.60	4771	2466000	42.0	<LOD	<LOD	48.0	0.010	0.002
	5	10.0	4884	2235000	Not Sampled			NA	NA	NA
	6	15.6	6542	2690000	144	<LOD	<LOD	150	0.023	0.006
	7	8.45	4392	2114000	176	<LOD	<LOD	182	0.041	0.009
	8	10.3	4995	2395000	45.0	<LOD	<LOD	51.0	0.010	0.002
	9	6.80	3813	1966000	45.0	<LOD	<LOD	51.0	0.013	0.003
	10	9.15	4625	2223000	46.0	<LOD	<LOD	52.0	0.011	0.002
	11	6.50	3703	2014000	75.0	<LOD	<LOD	81.0	0.022	0.004
	12	8.50	4408	2437000	32.0	<LOD	<LOD	38.0	0.009	0.002
	13	12.7	5708	2549000	26.0	<LOD	<LOD	32.0	0.006	0.001
	14	9.80	4836	2241000	34.0	<LOD	<LOD	40.0	0.008	0.002
	15	7.15	3940	2234000	169	<LOD	<LOD	175	0.044	0.008

Table 3. Propoxur Residues from Cotton Gloves Following 20 Petting Simulations to Treated Dogs										
Interval	Animal #	Animal Weight (kg)	Animal Surface Area (cm^2)	Actual Dose Applied[1] (µg ai)	Measured Residue on Gloves (µg/glove)			Total Residue[3]		% of applied dose transferred [4]
					Outer Cotton Glove #1[2]	Inner Cotton Glove #2[2]	Inner Cotton Glove #3[2]	µg/gloves	µg/cm^2 surface area of dog	
	16	7.90	4204	2220000	25.0	<LOD	<LOD	31.0	0.007	0.001
	17	6.20	3591	1964000	42.0	<LOD	<LOD	48.0	0.013	0.002

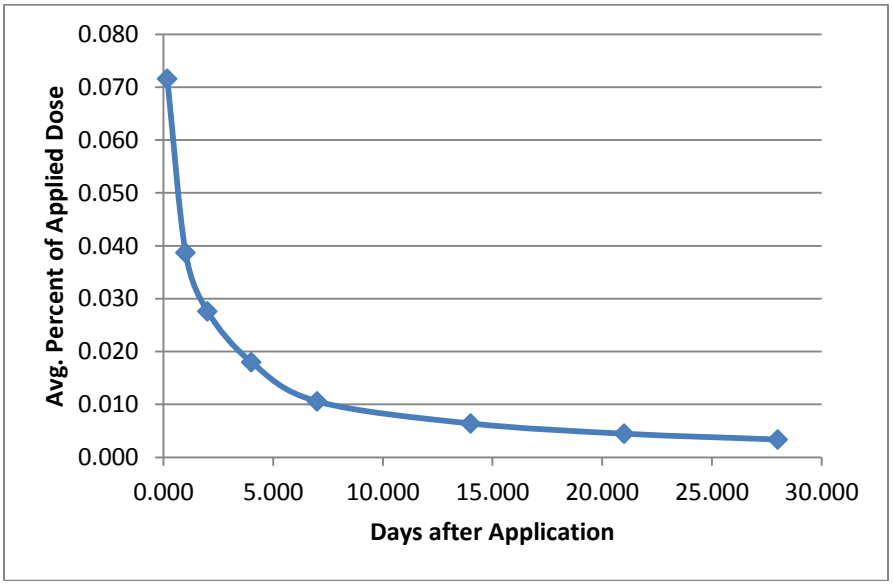
1. Applied Dose is based on a 10% of nominal collar application = (weight of collar applied to the dog at the beginning of the study)*0.10
2. LOD = 6 µg/glove and LOQ = 20 µg/glove. When residues were reported as less than the LOD or LOQ, Versar used a value of ½ LOD (3 µg/glove) or ½ LOQ (10 µg/glove) in the calculations.
3. Total Residue (µg/gloves) = outer cotton glove #1 + inner glove #2 + inner glove #3 (µg/glove). Total Residue (µg/cm^2) = Total residue on all 3 gloves / cm^2 body surface area of the dog.
4. % of applied dose transferred = Residue (µg/sample) / applied dose (µg ai) *100
5. Dog #5 was not sampled on Day 28 due to the handling of the dog during a seizure episode just prior to the sampling interval.

Table 4. Summary of Propoxur Residues from Cotton Gloves Following 20 Petting Simulations to Treated Dogs						
Interval	Total Residue				% of applied dose transferred[a]	
	µg/gloves		µg/cm^2 body surface area of dog			
	Average	Standard Deviation	Average	Standard Deviation	Average	Standard Deviation
4 hours	1626	613	0.359	0.124	0.072	0.025
1 day	877	515	0.195	0.118	0.039	0.023
2 days	622	397	0.140	0.091	0.028	0.018
4 days	407	289	0.091	0.067	0.018	0.013
7 days	241	147	0.054	0.035	0.011	0.007
14 days	145	85.5	0.032	0.018	0.006	0.004
21 days	102	64.9	0.022	0.012	0.004	0.003
28 days	76.6	53.3	0.017	0.012	0.003	0.002

Note: Totals represent sum of three cotton gloves. Gloves 4 and 5 were not quantified because 3rd inner glove residues were all <LOD. One of the dogs (Dog #5) was not sampled on Day 28.

a % of applied dose transferred = total µg ai in all gloves of one dog / µg ai applied to the dog

Figure 1. Percent of Applied Dose that was Transferred for Propoxur



Appendix A

Compliance Checklist

COMPLIANCE CHECKLIST

This compliance checklist is based on applicable criteria of the OPPTS Test Guidelines Series 875, Occupational and Residential Exposure Test Guidelines, Group B: 875.2300 (indoor surface residue) and OPPTS Test Guidelines Series 875, Occupational and Residential Exposure Test Guidelines, Group B: 875.2400 (dermal exposure).

1. *The test substance must be the typical end use product of the active ingredient.* This criterion was met.

2. *The production of metabolites, breakdown products, or the presence of contaminants of potential toxicologic concern, should be considered on a case-by-case basis.* This criterion was not met. Samples were analyzed for propoxur only and no discussion of production of metabolites or breakdown products was provided.

3. *Indoor surface residue studies should be conducted under ambient conditions similar to those encountered during the intended use season, and should represent reasonable worst case conditions.* This criterion does not apply.

4. *Ambient conditions (i.e., temperature, barometric pressure, ventilation) should be monitored.* This criterion was met.

5. The *end use product should be applied by the application method recommended on the label.* This criterion was met.

6. *The application rate used in the study should be provided and should be the maximum rate specified on the label. However, monitoring following application at a typical application rate is more appropriate in certain cases.* All dogs received the label recommended rate. The test product is a one size fits all flea and tick collar and actual dose was dependant on how the collar was attached and adjusted prior to cutting off the excess. The same person put all the collars on the dogs for consistency.

7. *If multiple applications are made, the minimum allowable interval between applications should be used.* This criterion does not apply. Only one application was made.

8. *Indoor surface residue (ISR) data should be collected from several different types of media (e.g., carpeting, hard surface flooring, counter tops, or other relevant materials).* This criterion does not apply.

9. *Sampling should be sufficient to characterize the dissipation mechanisms of the compound (e.g., three half-lives or 72 hours after application, unless the compound has been found to fully dissipate in less time; for more persistent pesticides, longer sampling periods may be necessary). Sampling intervals may be relatively short in the beginning and lengthen as the study progresses. Background samples should be collected before application of the test substance occurs.* This criterion was met.

10. *Triplicate, randomly collected samples should be collected at each sampling interval for each surface type.* This criterion was met. Fifteen replicates were collected at each sampling interval.

11. *Samples should be collected using a suitable methodology (e.g., California Cloth Roller, Polyurethane Roller, Drag Sled, Coupons, Wipe Samples, Hand Press, vacuum cleaners for dust and debris, etc.) for indoor surfaces.* This criterion was met. Samples were collected using cotton and nitrile gloves over a mannequin hand. Each sample consisted of 20 petting simulations with three strokes per simulation. The sample collection method followed the US EPA Science Advisory Council for Exposure Draft Guidance Document for Development of

12. *Samples should be stored in a manner that will minimize deterioration and loss of analytes between collection and analysis. Information on storage stability should be provided.* This criterion met. Information on storage stability was provided in a separate report supporting the stability of propoxur for 21 days of frozen storage. Samples were stored for a maximum of 11 days from collection to analysis.

13. *Validated analytical methods of sufficient sensitivity are needed. Information on method efficiency (residue recovery), and limit of quantitation (LOQ) should be provided.* This criterion was met. The validated LOD and LOQ were provided.

14. *Information on recovery samples must be included in the Study Report. A complete set of field recoveries should consist of at least one blank control sample and three or more each of a low-level and high-level fortification. These fortifications should be in the range of anticipated residue levels in the field study*. This criterion was met.

15. *Raw residue data must be corrected if appropriate recovery values are less than 90 percent.* This criterion was not required. Field fortification sample recoveries were all greater than 90%; therefore field sample residues did not require correction for field fortification recoveries.

16. *The monitoring period should be of sufficient duration to result in reasonable detectability on dosimeters. Monitoring should be conducted before residues have dissipated beyond the limit of quantification. Baseline samples should be collected before the exposure activity commences.* These criteria were met. Baseline samples were collected prior to putting collars on the dogs. Control samples were also collected from two dogs at each sampling interval. Propoxur residues were <LOD in all baseline and control samples.

17. *Activities monitored must be clearly defined and representative of typical practice.* This criterion was partially met. The activity of petting a dog is a typical post-application activity.

18. *Sufficient control samples should be collected.* This criterion was met. Two dogs were used as control dogs throughout the study.

Appendix B

Regression

Regression Analysis: Summary Output for Propoxur

Regression Statistics	
Multiple R	0.808315
R Square	0.653374
Adjusted R^2	0.650411
Standard Error	0.698649
Observations	119

ANOVA

	df	*SS*	*MS*	*F*	*Signif. F*
Regression	1	107.6474	107.6474	220.53915	1.09479E-28
Residual	117	57.10888	0.48811		
Total	118	164.7563			

	Coeff.	*Std. Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*
Intercept	-3.47564	0.090281	-38.4979	2.789E-68	-3.65443281	-3.296838448
Slope	-0.09956	0.006704	-14.8506	1.095E-28	-0.112834255	-0.086280608

Half Life = 6.962285 Days

Predicted Concentration Levels

Time (Days)	Residue (% of applied dose)
0	0.030942
1	0.02801
2	0.025356
3	0.022953
4	0.020778
5	0.018809
6	0.017027
7	0.015413
8	0.013953
9	0.01263
10	0.011433
11	0.01035
12	0.009369
13	0.008481
14	0.007678
15	0.00695
16	0.006292
17	0.005695
18	0.005156
19	0.004667
20	0.004225

Time (Days)	Residue (% of applied dose)
21	0.0038244
22	0.003462
23	0.003134
24	0.002837
25	0.0025681
26	0.0023248
27	0.0021045
28	0.0019051
29	0.0017245
30	0.0015611
31	0.0014132
32	0.0012793
33	0.001158
34	0.0010483
35	0.000949

Regression Analysis: Means and CVs for Propoxur

Days after Last Treatment	Residues (% of applied dose)	Mean (% of applied dose)	Standard Deviation (% of applied dose)	Coefficient of Variation (%)
0.167	0.06	0.0716	0.0251	35.1
	0.08			
	0.05			
	0.13			
	0.07			
	0.05			
	0.11			
	0.035			
	0.07			
	0.08			
	0.05			
	0.06			
	0.05			
	0.07			
	0.10			
1	0.031	0.0387	0.0226	58.4
	0.043			
	0.020			
	0.07			
	0.032			
	0.023			
	0.07			
	0.013			
	0.04			
	0.06			
	0.024			
	0.032			
	0.018			
	0.018			
	0.08			
2	0.017	0.0276	0.0175	63.6
	0.014			
	0.012			
	0.06			
	0.030			
	0.011			
	0.043			
	0.011			
	0.026			
	0.043			
	0.016			
	0.024			
	0.031			
	0.013			
	0.067			
4	0.014	0.018	0.0128	71.3

	0.006			
	0.012			
	0.04			
	0.017			
	0.015			
	0.020			
	0.005			
	0.013			
	0.023			
	0.009			
	0.015			
	0.026			
	0.005			
	0.051			
7	0.007	0.0106	0.00653	61.6
	0.006			
	0.007			
	0.019			
	0.008			
	0.006			
	0.010			
	0.003			
	0.009			
	0.015			
	0.011			
	0.009			
	0.019			
	0.004			
	0.026			
14	0.009	0.00641	0.00352	54.9
	0.003			
	0.005			
	0.014			
	0.009			
	0.003			
	0.007			
	0.002			
	0.008			
	0.006			
	0.002			
	0.004			
	0.010			
	0.004			
	0.011			
21	0.004	0.00449	0.00255	56.7
	0.002			
	0.003			
	0.011			
	0.006			
	0.002			
	0.004			
	0.003			

	0.008			
	0.003			
	0.002			
	0.004			
	0.006			
	0.003			
	0.005			
28	0.004	0.00333	0.00242	72.6
	0.002			
	0.006			
	0.009			
	0.002			
	0.003			
	0.002			
	0.004			
	0.002			
	0.001			
	0.002			
	0.008			
	0.001			
	0.002			

Regression Analysis: Log of Concentration vs. Time for Propoxur